Veterinary Dermatology
Dermatologie vétérinaire

Use of topical glucocorticoids in veterinary dermatology

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Introduction

Topical glucocorticoids (TGC) are among the oldest and most efficient treatments to control inflammatory and immune-mediated skin disorders (1). In veterinary medicine, TGC are less attractive than in human medicine due to the density of hair and pet behavior (pets often lick the area where the topicals are applied). Moreover, the extent of body regions to be covered and the cost of topicals might, in some cases, be considered by veterinarians as limitations for the use of TGC (2). Ear disease is probably the most common reason to prescribe TGC in veterinary medicine. The greatest advantage of using TGC is the few adverse effects associated with this route of administration (2–5).

Selecting the proper TGC is not easy. Indeed, whether the goal is to treat otitis externa or to address inflamed skin, the TGC chosen will affect the outcome since they vary in potency, formulation, and side effects.

Properties of topical corticosteroids

Anti-inflammatory properties vary according to the corticosteroid used. Although several mechanisms of action have been proposed, the exact mechanism of action of TGC is unclear. Some studies have shown that TGC impact proinflammatory molecules and mediators of pruritus, inflammation-associated nerve hypersensitivity, as well as recruitment of inflammatory cells. Topical glucocorticoids interfere with the inflammatory process and pruritogenic pathway by inhibiting the arachidonic acid pathway, some inflammatory cytokines and growth factors, and decreasing the expression of some adhesion molecules (3,6). The anti-inflammatory potency is often proportional

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Conflicts of interest: In the last 5 years, Frédéric Sauvé has received honoraria, consulting fees, and/or collaborated with Royal Canin, Zoetis, and Elanco.

to the ability of the corticosteroid to cause suppression of the hypothalamic-pituitary-adrenal axis and the severity of its side effects (3). Interestingly, the liver must activate the cortisone and prednisone in cortisol and prednisolone, respectively, to be metabolically active. Their topical use is therefore inappropriate (3). In North America, TGC are divided into 7 classes based on their ability to cause vasoconstriction (skin blanching in healthy people) (1,7). Class 1 contains the most potent molecules, whereas class 7 groups the weakest molecules (8). The beneficial effects obtained, as well as the side effects, also vary according to the vehicle of the product, the site of application, the disease being addressed, and individual response (1).

Choosing the proper topical glucocorticoid

There is no doubt that TGC can be very useful for treating inflammatory skin disorders, especially if the dermatitis is localized, but care must be taken to choose the appropriate formulation for the patient. The choice of TGC should be based on patient factors as well as properties of the selected product. Briefly, selection of TGC depends on the dermatosis addressed, the extent of the surface to be treated, the skin site, and the health status of the animal (1,7). The first step for a successful response to TGC is to properly identify the dermatitis being treated. Not all inflamed skin requires TGC. Indeed, a generalized demodicosis or a skin infection might cause significant skin inflammation. However, the use of glucocorticoids (GC) in the presence of these skin diseases is usually contraindicated (9). Other than otitis externa, immune-mediated skin disorders and irritant or allergic skin diseases are the most common reasons for prescribing TGC. The potency of the GC chosen is also important (1,7). The GC selected to treat an inflammation caused by a mild contact dermatitis or a pemphigus foliaceus should differ from one another. In most cases, immune-mediated skin diseases require more potent GC than an allergic or irritant dermatitis.

Based on the North American classification of TGC, mild GC (classes 6 and 7) are preferred when the lesions are mildly inflamed, a large area has to be treated, or the skin is thin at the site of application (e.g., axillae and groins) (1,7). These classes are also preferred for long-term use (1). The moderate to potent GC (classes 3 to 5) are selected when the dermatitis is moderately to severely inflamed, discomfort is moderate to severe, or in areas where the skin is thick (e.g., calluses, foot pads, nasal planum) (7). Finally, GC classified as potent to very potent (classes 2 and 1) must not be used in areas where the skin is thin or under occlusion (1). They should be prescribed for very severe skin disorders and for a short time (no more than 3 weeks) (1,7). The topicals' properties, such as the delivery vehicle, must also be considered as well as the duration of treatment and the potential side effects (1,3,7,9). Although the occlusive nature of an ointment improves GC absorption, it may also cause maceration if used in occluded areas (skin folds, high hair density, interdigital spaces). Ointments are appropriate for lichenified or hyperkeratotic surface because they are occlusive and provide better lubrication (1,7,9). Creams (mixes of water suspended in oil) are usually cosmetically more acceptable and have moisturizing properties. They are indicated for exudative inflammation, such as intertrigo, or in hairy areas (1,7,9).

Table 1. Potency of otic preparations containing glucocorticoids (GC) (1,8,9).

Otic preparation	Glucocorticoids	Potency (American classification)
Claro® Bayer Animal Health, Mississauga, Ontario	Mometasone furoate 0.22% (solution)	Potent (?)
Mometamax® Merck Animal Health, Kirkland, Quebec	Mometasone furoate 0.1% (suspension)	Potent (2 to 3)
Otomax® Merck Animal Health, Kirkland, Quebec	Betamethasone valerate 0.1% (ointment)	Upper mid-strength (3)
Osurnia® Elanco Animal Health, Guelph, Ontario	Betamethasone acetate 0.1% (gel)	Upper mid-strength (?)
Aurizon® Vétoquinol, Lavaltrie, Quebec	Dexamethasone acetate 0.09% (suspension)	Mid-strength (4 to 5)
Tresaderm® Boehringer Ingelheim, Burlington, Ontario	Dexamethasone 0.1% (solution)	Mild/Mid-strength (5 to 6)
Surolan® Elanco Animal Health, Guelph, Ontario	Prednisolone acetate 0.5% (suspension)	Mild (~6)
Otizole® ProConcepts, Mississauga, Ontario	Prednisolone acetate 0.5% (suspension)	Mild (~6)
Canaural® Dechra Veterinary Products, Pointe-Claire, Quebec	Prednisolone acetate 0.25% (suspension)	Mild (~6)

Note that the data in the literature are not always clear and concordant regarding the exact classification of the potency of topical GCs. This table is only indicative of the relative potency of each GC.

However, creams are usually less potent than ointments, even if they contain the same chemical formulation of GC (1). Creams contain preservatives, which may cause a local cutaneous reaction (1,7). Lotions, gels, and foams containing GC are not commonly used in veterinary dermatology. Lotions which contain alcohol and gels are less greasy and dry quickly (1,7). Whatever the delivery vehicle chosen, it is not recommended that the TGC be applied more than twice a day (1). An example of a topical product approved in human medicine, but often misused in veterinary medicine, is a mixture of triamcinolone acetonide, gramicidin, neomycin, and nystatin (Viaderm KC; Taro Pharmaceuticals, Brampton, Ontario). The triamcinolone acetonide within the cream or ointment version is considered a class 3 GC (10). Such a high potent GC is required only if the inflammation is severe, the epidermis is hyperkeratotic, the animal is highly pruritic, or in pain. In addition, it should not be used for a prolonged period, especially in areas of thin skin. Unfortunately, the misuse of this product highly increases the risk of local and systemic side effects.

On the Canadian veterinary market, there are 5 topicals containing GC that are licensed to be used on the skin: 3 sprays, 1 gel, and 1 cream. Among sprays, there are a 1% hydrocortisone spray (CortiPro; ProConcepts, Mississauga, Ontario), a

Table 2. Local side effects reported with the use of topical glucocorticoids (1,3,9).

Cutaneous atrophy
Alopecia
Comedones
Prominent dermal blood vessels
Phlebectasia (vascular proliferation and dilatation)
Purpura
Subepidermal bulla
Hypopigmentation
Delayed wound healing
Bacterial pyoderma, demodecosis
Cutaneous calcinosis
Scaling
Pinnal curling

hydrocortisone aceponate spray (Cortavance; Virbac, Cambridge, Ontario), and a gentamicin sulfate and betamethasone valerate spray (Topagen spray; Merck Animal Health, Kirkland, Quebec). Hydrocortisone is considered to be the weakest TGC (class 7) (8). Hydrocortisone spray is indicated for mild inflammation, as an adjunctive treatment to decrease doses of oral anti-inflammatory drugs, and for long-term use. Hydrocortisone has a low potential of side effects, even on thin skin areas. Hydrocortisone aceponate is not equivalent to hydrocortisone. Due to its lipophilic property, the hydrocortisone aceponate accumulates within the skin, which gives a higher potential for local action (9). The chemical properties of hydrocortisone aceponate increase its potency to the moderate level (classes 4 to 5) (9,11). Systemic side effects are uncommon because of its low plasma bioavailability (9,10). One study failed to show significant side effects after 28 d when applied once daily (12). Another study didn't show systemic side effects, but there was skin atrophy following 14 d of daily application (11). Several types of dermatitis may benefit from hydrocortisone aceponate such as skin allergies, pododermatitis, intertrigo, and otitis. Although the long-term use of hydrocortisone aceponate is considered relatively safe, it shouldn't be applied on the skin daily for a prolonged period (11). In maintenance, hydrocortisone aceponate may be used 2 times per week to prevent flare-up of cutaneous allergic diseases or recurrent inflammatory otitis (2,6,10). The spray combining gentamicin sulfate and betamethasone valerate should be used cautiously. In fact, betamethasone valerate is an upper mid-strength GC (class 3). It has a high potential for local and systemic side effects. Its use should, therefore, be short-lived in cases of severe inflammation, pruritus or pain, especially if a bacterial infection is present concomitantly.

Other topical veterinary products containing GC include a combination of fusidic acid and betamethasone valerate in a gel form (Isaderm gel; Dechra Veterinary Products, Pointe-Claire, Quebec), and a cream with a mixture of triamcinolone acetonide, nystatin, neomycin, and gramicidin (Theraderm; Bimeda, Cambridge, Ontario). The potency of both GC found in these topicals is in the upper mid-strength class (class 3) (8). As for the other TGC from this class or higher classes, they should be used with the same regard concerning the location of skin lesions, duration of therapy, integrity of the skin barrier, and density of hairs. The topical products combining antibiotics and GC might be helpful in quickly calming the pruritus or pain in the presence of bacterial pyoderma. However, they should never be considered as a sole therapy to treat such disease. The presence of the GC will delay healing and may affect resolution of bacterial infection by altering the local skin immune system. Moreover, the quick decrease of the inflammation gives a false impression that the bacterial infection is under control, often resulting in too short a duration of a treatment.

Immune-mediated dermatoses may benefit from upper mid-strength (class 3), potent (class 2), or superpotent (class 1) TGC as sole or adjunctive therapy. The main purpose of TGC in veterinary medicine is probably the treatment of otitis externa. The potency of the GC differs among otic preparations. A summary of otic preparations containing GC is presented in Table 1. As for skin diseases, the properties of GC in otic preparations must be considered before making a selection. In the presence of severe otitis and/or evidence of stenosis or ceruminous gland hyperplasia, an otic preparation containing a class 2 to 3 GC should be selected. The inflammation and itchiness caused by a mild otitis externa (e.g., yeast or bacterial overgrowth, mild allergic or ceruminous otitis) should be controlled by a class 4 to 6 GC. Pain might also be a factor to consider when choosing the potency of GC for treating otitis externa.

Adverse effects of TGC

Unfortunately, these topical therapies may cause side effects. Indeed, local cutaneous effects as well as their systemic absorption (especially if the skin barrier is disrupted) may be important (9). Several studies have shown that different veterinary otic and ophthalmic preparations containing GC, as well as ointment applied topically on the dorsal cervical skin of dogs, may cause significant suppression of the hypothalamic-pituitary-adrenal axis (3,9,13–17). This suppression may persist for up to 4 wk after the local treatment has been stopped (15). Systemic side effects (clinical signs mimicking hyperadrenocorticism) may occur following transcutaneous absorption (15,17). There are also numerous potential local adverse effects that are summarized in Table 2. Local cutaneous side effects vary according to the potency of the TGC used, the duration of treatment, the skin site treated, volume of the topical applied, and the patient's susceptibility (7). The most common side effect reported in human dermatology associated with the local use of GC is skin atrophy (1). Skin atrophy, comedones, alopecia, skin infection, scaling, and calcinosis cutis are common local side effects associated with the use of TGC in veterinary medicine. Long-term use of TGC on pinnae of cats may also cause pinnal curling (9).

In conclusion, topical GCs are very useful and effective if they are prescribed wisely (4,5). Although no single agent has been proven to have the best benefit-to-risk ratio, the adverse reactions and beneficial effects are minimized and optimized, respectively, when the diagnosis, the potency of GCs, and their delivery vehicles, the area treated, and the duration of the treatment are considered before selection of the TGC (1,7,9). Immunological, inflammatory, including burning and pruritic sensations, and hyperproliferative disorders may all benefit from TGC (1,7) as long as the topicals are in direct contact with the skin, the animal doesn't lick the area treated, and the lesions are not too extensive. If the skin disorder does not improve

or if it worsens, it is important to recheck the patient for skin microbial infection or parasitic infestation, before considering a systemic approach.

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